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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,765	12/29/2003	Illana Gozes	019856-000210US	8714

20350 7590 07/06/2006

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EXAMINER	
WOODWARD, CHERIE MICHELLE	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 07/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/748,765	GOZES ET AL.	
	Examiner	Art Unit	
	Cherie M. Woodward	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *2-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 9-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7 October 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II (claims 1-28 as drawn to SEQ ID NO: 2) in the reply filed on 11 April 2006 is acknowledged. The traversal is on the grounds that it would not be a burden for the examiner to examine all 12 SEQ ID NOs at one time. This is not found persuasive because each of the SEQ ID NOs are unique and patentably distinct, requiring a separate search of the prior art. Searching all of the sequences in a single patent application would constitute an undue search burden on the examiner and the USPTO's resources because of the potentially non-coextensive nature of these searches. The requirement is still deemed proper and is therefore made FINAL.

Formal Matters

2. In the Response filed 11 April 2006, Applicants state that the elected SEQ ID NO: 2 reads on claims 1 and 9-28. Claims 1-28 are pending. Claims 2-8 are withdrawn, as being drawn to non-elected inventions. Claims 1 and 9-28 are under examination.

Objections to the Specification

3. The disclosure is objected to because of the following informalities: Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The first paragraph (01) of the disclosure states that the application "claims priority to a provisional US Application 60/647,650 filed 2 January 2003." The proper phrasing is a claim for benefit, not for priority.

Additionally, the reference to the documents recited in paragraph 02 of the specification (page 1) is improper. The listed documents are not "related" to the instant application by way of priority or benefit. Appropriate correction is required.

Incorporation by Reference

4. Applicant incorporates by reference the full sequence of ADNF III polypeptides by citing two WO documents by reference (p. 5, lines 15 and 16 of the specification). There are numerous ADNF III polypeptides known in the art (see attached NCBI reports) for different species. It is unclear from the

incorporation by reference which ADNF III polypeptide Applicant is referring to in the referenced WO documents or whether the referenced WO documents contain multiple ADNF III sequences, and if so, which one(s) are claimed. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. Additionally, in doing so, Applicant must comply with the Sequence Rules, see 37 CFR 1.821- 1.825, MPEP 2420. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

Claim Objections

5. Claims 1, 14, 17-22 are objected to because of the following informalities: the claims contain subject matter directed to non-elected inventions. Appropriate correction is required.

6. Claims 15 and 22 are objected to because of the following informalities: the claims contain the phrase "...about 20 amino acids at at least one...." It is believed that the "at at" is a typographical error. The "at at" phrase occurs twice in claim 22, on lines 2 and 4. Appropriate correction is required.

7. Claim 25 is objected to because of the following informalities: septic shock is not an autoimmune disease. It is an immune reaction, but not an autoimmune disease. Appropriate correction is required.

Claim Rejections - 35 USC § 112, First Paragraph
Scope of Enablement

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 9-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating neurologically-related autoimmune diseases by administering to a subject a therapeutically effective amount of the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for treating an autoimmune disease by administering the full length ADNF III polypeptide or for preventing an autoimmune disease via administering either the polypeptide of SEQ ID NO:2 or the

full length ADNF polypeptide. Additionally, while being enabling for treating neurologically-related autoimmune diseases, neither the specification nor the art reasonably provide enablement for treating or preventing all autoimmune diseases of claim 25. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working samples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims recite a method for preventing or treating an autoimmune disease in a subject, comprising administering to the subject a therapeutically effective amount of an Activity-Dependent Neurotrophic Factor (ADNF) polypeptide, wherein the ADNF polypeptide is a member selected from the group consisting of an ADNF polypeptide comprising an active core site having the following amino acid sequence: NAPVSIPQ (SEQ ID NO: 2) [as elected]; wherein the ADNF polypeptide is an ADNF III polypeptide; wherein the ADNF polypeptide is a full length ADNF III polypeptide; wherein the ADNF III polypeptide is SEQ ID NO: 2; wherein the active core site of the ADNF III polypeptide comprises at least one D-amino acid; wherein the active core site of the ADNF III polypeptide comprises all D-amino acids; wherein the ADNF III polypeptide is a member of the group consisting of SEQ ID NO: 2 [as elected]; wherein the ADNF III polypeptide comprises up to about 20 amino acids at at [sic] least one f the N-terminus and the C-terminus of the active core site; wherein at least one of the ADNF polypeptides is encoded by a nucleic acid that is administered to the subject; wherein an ADNF I polypeptide of part (a) and an ADNF III polypeptide of part (b) are administered to the subject; wherein either or both active core sites of the ADNF I polypeptide and the ADNF III polypeptide comprise at least one D-amino acid; wherein either or both active core sites of the ADNF I polypeptide and the ADNF III polypeptide comprise all D-amino acids; wherein the ADNF I polypeptide is SEQ ID NO: 1 and wherein the ADNF III polypeptide is SEQ ID NO: 2; wherein the ADNF I polypeptide is a member of the group consisting of SEQ ID NO:1 and the ADNF III polypeptide is selected from the group consisting of SEQ ID NO: 2; wherein the ADNF I polypeptide comprises up to about 20 amino acids at at [sic] least one of the N-terminus and the C-terminus of the active core site of the ADNF I polypeptide and wherein the ADNF III polypeptide comprises up to about 20 amino acids at at [sic] least one of the N-terminus and the C-

terminus of the active core site of the ADNF III polypeptide; wherein the subject has an autoimmune disease; wherein the ADNF polypeptide is administered to prevent an autoimmune disease; wherein the autoimmune disease is Guillan-Barre syndrome; wherein the ADNF polypeptide is administered intanasally; wherein the ADNF polypeptide is administered orally; wherein the ADNF polypeptide is injected.

The nature of the invention is drawn to a method for administering an ADNF III polypeptide comprising an active core site comprising the sequence of SEQ ID NO: 2 (NAPVSIPQ) in a subject to prevent or treat an autoimmune disease, such as Guillan-Barre. However, the claims are also drawn to the full length ADNF III polypeptide. The claimed full length ADNF III polypeptide is not taught in the instant specification. However, Applicant attempts to incorporate the full length ADNF III sequence by reference to two WO documents ((p. 5, lines 15 and 16 of the specification). Even so, there are multiple known sequences for multiple ADNF III polypeptides in the same (i.e. polymorphisms) and different species. For example, see NCBI entries: NP_033785, a 1108 amino acid sequence of activity-dependent neuroprotective peptide from mice; BAE22284 a 1108 amino acid sequence with accession number AK134786.1 from mice; BAA34504, a 1073 amino acid sequence with accession number AB018327.1 from human brain tissue; and AAH75794, a 1102 amino acid sequence with accession number BC075794.1 from human cDNA clones. Although multiple full-length ADNF III sequences from different species are known in the art that comprise an active core site having the amino acid sequence of SEQ ID NO: 2 (NAPVSIPQ), neither the instant disclosure nor the claims teach which, of the many full-length ADNF III sequences, a skilled artisan should use to make or practice the instant invention.

Further, while being enabling for treating neurologically-related autoimmune diseases, neither the specification nor the art reasonably provide enablement for treating or preventing all autoimmune diseases of claim 25. Many of the autoimmune diseases of claim 25 are B-cell/antibody based autoimmune diseases or have an unknown etiology. Moreover, septic shock, for example, is not an autoimmune disease. It is an immune reaction (or over-reaction) resulting from infection, but it is not a chronic disease whereby the immune system of a subject is activated against self-antigens. Septic shock is specifically related to the immune system's reaction to foreign antigens, primarily bacterial antigens.

Additionally, the specification does not reasonably provide enablement for prevention of an autoimmune disease in a subject. The skilled artisan cannot envision the prevention of an autoimmune disease. Prevention involves "attacking" the underlying cause of autoimmune disease; i.e., disrupting the mechanisms which give rise to autoimmune disease. The skilled artisan is aware that the causes of almost every autoimmune disease were unknown at the time of the invention herein. For purposes of

enablement, the specification must provide reasonable detail in order for those skilled in the art to carry out the invention. In this case, the specification must disclose a means of preventing autoimmune diseases regardless of the underlying causes of the autoimmune disease. The teachings of the specification do not enabled a person of ordinary kill in the art to make and use the claimed method of prevention. Moreover, "[p]atent protection is granted only in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable." Genentech Inc. v. Novo Nordisk A/S, 108 F.3d at 1366, 42 USPQ2d at 1005 (Fed. Cir.), cert. denied, 118 S. Ct. 397 (1997), ("Tossing out the mere germ of an idea does not constitute an enabling disclosure").

Therefore, based on the discussions above concerning the art's recognition that the diversity of full-length ADNF III polypeptides with an active core sequence comprising SEQ ID NO: 2, the specification fails to teach the skilled artisan how to use the claimed methods without resorting to undue experimentation. Due to the large quantity of experimentation necessary to determine which full-length ADNF III polypeptide from any species, such that it can be determined how to use the claimed methods, the lack of direction/guidance presented in the specification regarding same, the absence of sufficient working examples directed to same, the complex nature of the invention, the state of the prior art establishing that there are numerous full-length ADNF III polypeptides from different species, each consisting of a different amino acid sequence, and the breadth of the claims which fail to recite the specific species or sequence of full-length ADNF III polypeptide to use in the method, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, First Paragraph

Written Description

10. Claims 1 and 9-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims recite a method for preventing or treating an autoimmune disease in a subject, comprising administering to the subject a therapeutically effective amount of an Activity-Dependent Neurotrophic Factor (ADNF) polypeptide, wherein the ADNF polypeptide is a member selected from the

group consisting of an ADNF polypeptide comprising an active core site having the following amino acid sequence: NAPVSIPQ (SEQ ID NO: 2) [as elected]; wherein the ADNF polypeptide is an ADNF III polypeptide; wherein the ADNF polypeptide is a full length ADNF III polypeptide; wherein the ADNF III polypeptide is SEQ ID NO: 2; wherein the active core site of the ADNF III polypeptide comprises at least one D-amino acid; wherein the active core site of the ADNF III polypeptide comprises all D-amino acids; wherein the ADNF III polypeptide is a member of the group consisting of SEQ ID NO: 2 [as elected]; wherein the ADNF III polypeptide comprises up to about 20 amino acids at at [sic] least one f the N-terminus and the C-terminus of the active core site; wherein at least one of the ADNF polypeptides is encoded by a nucleic acid that is administered to the subject; wherein an ADNF I polypeptide of part (a) and an ADNF III polypeptide of part (b) are administered to the subject; wherein either or both active core sites of the ADNF I polypeptide and the ADNF III polypeptide comprise at least one D-amino acid; wherein either or both active core sites of the ADNF I polypeptide and the ADNF III polypeptide comprise all D-amino acids; wherein the ADNF I polypeptide is SEQ ID NO: 1 and wherein the ADNF III polypeptide is SEQ ID NO: 2; wherein the ADNF I polypeptide is a member of the group consisting of SEQ ID NO:1 and the ADNF III polypeptide is selected from the group consisting of SEQ ID NO: 2; wherein the ADNF I polypeptide comprises up to about 20 amino acids at at [sic] least one of the N-terminus and the C-terminus of the active core site of the ADNF I polypeptide and wherein the ADNF III polypeptide comprises up to about 20 amino acids at at [sic] least one of the N-terminus and the C-terminus of the active core site of the ADNF III polypeptide; wherein the subject has an autoimmune disease; wherein the ADNF polypeptide is administered to prevent an autoimmune disease; wherein the autoimmune disease is Guillan-Barre syndrome; wherein the ADNF polypeptide is administered intanasally; wherein the ADNF polypeptide is administered orally; wherein the ADNF polypeptide is injected.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117). A review of the language of the claim indicates that these claims are drawn to a genus.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states, "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

The nature of the invention is drawn to a method for administering an ADNF III polypeptide comprising an active core site comprising the sequence of SEQ ID NO: 2 (NAPVSIPQ) in a subject to prevent or treat an autoimmune disease, such as Guillan-Barre. However, the claims are also drawn to the full length ADNF III polypeptide. The claimed full length ADNF III polypeptide is not taught in the instant specification. However, Applicant attempts to incorporate the full length ADNF III sequence by reference to two WO documents ((p. 5, lines 15 and 16 of the specification). Even so, there are multiple known sequences for multiple ADNF III polypeptides in the same (i.e. polymorphisms) and different species. For example, see NCBI entries: NP_033785, a 1108 amino acid sequence of activity-dependent neuroprotective peptide from mice; BAE22284 a 1108 amino acid sequence with accession number AK134786.1 from mice; BAA34504, a 1073 amino acid sequence with accession number AB018327.1 from human brain tissue; and AAH75794, a 1102 amino acid sequence with accession number BC075794.1 from human cDNA clones. Although multiple full-length ADNF III sequences from different species are known in the art that comprise an active core site having the amino acid sequence of SEQ ID NO: 2 (NAPVSIPQ), neither the instant disclosure nor the claims disclose which, of the many known full-length ADNF III sequences describe the claimed full-length ADNF III polypeptide.

Neither the specification nor the claims indicate which members of the genus of the different ADNF III polypeptides described in the art were in the possession of the inventors at the time of filing. The genus of ADNF III polypeptides is highly variant (as shown from the different ADNF III polypeptides above) because a significant number of structural differences between genus members has been reported. The instant disclosure fails to provide an adequate description of any specific ADNF III

polypeptide from any specific species. The general knowledge and level of those of ordinary skill do not supplement the omitted description because specific, not general, descriptions are needed. Because the disclosure fails to adequately describe which full-length ADNF III polypeptide is claimed, and because the genus is variant, depending on the species, a full-length ADNF III polypeptide comprising an active core site having the amino acid sequence of SEQ ID NO: 2, is insufficient to describe the genus of ADNF III polypeptides. Thus, one of skill would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. As such, it appears that Applicant was not in possession of the claimed genus at the time the application was filed.

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is a therapeutic agent, a reference molecule, and a therapeutic index. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, Second Paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1 and 9-28 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims are incomplete for omitting essential steps. While all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. The minimum requirements for method steps include a contacting step in which the reaction of the sample with the reagents necessary for the assay is recited, a detection step in which the reaction steps are quantified or visualized, and a correlation step describing how the results of the assay allow for the determination. In the present case, the claims are missing a correlation step.

13. Claims 15 and 22 rejected as failing to define the invention in the manner required by 35 U.S.C. 112, second paragraph. The claims are so unclear that the Examiner cannot determine what the Applicant

is attempting to claim. The claims are narrative in form and replete with indefinite and functional or operational language. The structure which is asserted to make up the polypeptide must be clearly and positively specified. The structure must be organized and correlated in such a manner as to present a complete operative embodiment which has support in the specification. The claims must be in one sentence form only. Note the format of the claims in the patents cited below.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 1, 9-11, 14-15, 17, and 20-28 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by WO 98/35042 (published 13 August 1998).

The claims recite a method for preventing or treating an autoimmune disease in a subject, comprising administering to the subject a therapeutically effective amount of an Activity-Dependent Neurotrophic Factor (ADNF) polypeptide, wherein the ADNF polypeptide is a member selected from the group consisting of an ADNF polypeptide comprising an active core site having the following amino acid sequence: NAPVSIPQ (SEQ ID NO: 2) [as elected]; wherein the ADNF polypeptide is an ADNF III polypeptide; wherein the ADNF polypeptide is a full length ADNF III polypeptide; wherein the ADNF III polypeptide is SEQ ID NO: 2; wherein the active core site of the ADNF III polypeptide comprises at least one D-amino acid; wherein the active core site of the ADNF III polypeptide comprises all D-amino acids; wherein the ADNF III polypeptide is a member of the group consisting of SEQ ID NO: 2 [as elected]; wherein the ADNF III polypeptide comprises up to about 20 amino acids at at [sic] least one f the N-terminus and the C-terminus of the active core site; wherein at least one of the ADNF polypeptides is encoded by a nucleic acid that is administered to the subject; wherein an ADNF I polypeptide of part (a) and an ADNF III polypeptide of part (b) are administered to the subject; wherein either or both active core sites of the ADNF I polypeptide and the ADNF III polypeptide comprise at least one D-amino acid; wherein either or both active core sites of the ADNF I polypeptide and the ADNF III polypeptide

comprise all D-amino acids; wherein the ADNF I polypeptide is SEQ ID NO: 1 and wherein the ADNF III polypeptide is SEQ ID NO: 2; wherein the ADNF I polypeptide is a member of the group consisting of SEQ ID NO:1 and the ADNF III polypeptide is selected from the group consisting of SEQ ID NO: 2; wherein the ADNF I polypeptide comprises up to about 20 amino acids at at [sic] least one of the N-terminus and the C-terminus of the active core site of the ADNF I polypeptide and wherein the ADNF III polypeptide comprises up to about 20 amino acids at at [sic] least one of the N-terminus and the C-terminus of the active core site of the ADNF III polypeptide; wherein the subject has an autoimmune disease; wherein the ADNF polypeptide is administered to prevent an autoimmune disease; wherein the autoimmune disease is Guillan-Barre syndrome; wherein the ADNF polypeptide is administered intanasally; wherein the ADNF polypeptide is administered orally; wherein the ADNF polypeptide is injected.

WO 98/35042 teaches method of using ADNF III polypeptides for the treatment and prevention of neurological deficiencies (abstract), including the amino acid sequence NAVPSIPQ (SEQ ID NO:6), [which is identical to instant SEQ ID NO: 2] and SALLRSIPA (SEQ ID NO: 5), [which is identical to instant SEQ ID NO: 1] (column 3, lines15-19 and 60-67; column 21, lines 15-18; column 44, lines 42-53; column 45, lines 32-). SALLRSIPA (SEQ ID NO: 5) is identified as an ADNF III polypeptide in the '740 Patent (column 20, lines 21-25). The protective effect of ADNF III polypeptides in preventing neuronal cell death is taught at column 3, lines 60-67. Full-length ADNF III is taught at column 3, lines 63-64. The administration of ADNF III polypeptides to prevent neuronal cell death associated with a number of other neurological diseases and deficiencies is taught at column 6, lines 33-36, and the use of ADNF III polypeptides to treat other neurological disorders is taught at column 6, lines 59-60. ADNF III variant polypeptides, including an ADNF III polypeptide comprising up to about 20 amino acids and at least one of the N-terminus and the C-terminus of the active core site are taught at column 3, lines 38-67 to column 4, lines 1-53; and column 45, lines 43-61; column 49, lines 47-49). Treatment of the neuro-autoimmune disease, Guillian-Barre syndrome, is taught at column 45, line 7. Amino acid sequences with naturally occurring amino acids and amino acid analogs, which include known analogues of natural amino acids that function in a manner similar to the naturally occurring amino acids (i.e. amino acid mimetics and analogs) are taught at column 5, lines 34-64. Administration of the ADNF III polypeptides systemically, intravenously, subcutaneously, intranasally, and orally are taught at column 45, lines 62-67 to column 46, lines 1-20; column 46, lines 31-37; and column 46, lines 60-65). The SALLRSIPA polypeptide, also identified as "ADNF-9" (at column 3, lines 60-61) is taught as being administered concurrently with "NAP" (NAPVSIPQ, SEQ ID NO: 6; taught as "NAP" at column 9, lines 6-7; column

7, line 44; column 59, lines 9-12) (column 60, lines 38-39). Administration of ADNF-14 (a polypeptide which comprises ADNF-9, see column 2, lines 63-64), ADNF-9, and NAP to mice are taught at Figure 16, column 10, lines 1-11; Figure 17, column 10, lines 12-23; and column 60, lines 31-53).

16. Claims 1, 9-11, 14-15, 17, and 20-28 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Gozes et al., US Patent 6,613,740 (2 September 2003, priority to 7 February 1997).

The claims recite a method for preventing or treating an autoimmune disease in a subject, comprising administering to the subject a therapeutically effective amount of an Activity-Dependent Neurotrophic Factor (ADNF) polypeptide, wherein the ADNF polypeptide is a member selected from the group consisting of an ADNF polypeptide comprising an active core site having the following amino acid sequence: NAPVSIPQ (SEQ ID NO: 2) [as elected]; wherein the ADNF polypeptide is an ADNF III polypeptide; wherein the ADNF polypeptide is a full length ADNF III polypeptide; wherein the ADNF III polypeptide is SEQ ID NO: 2; wherein the active core site of the ADNF III polypeptide comprises at least one D-amino acid; wherein the active core site of the ADNF III polypeptide comprises all D-amino acids; wherein the ADNF III polypeptide is a member of the group consisting of SEQ ID NO: 2 [as elected]; wherein the ADNF III polypeptide comprises up to about 20 amino acids at at [sic] least one f the N-terminus and the C-terminus of the active core site; wherein at least one of the ADNF polypeptides is encoded by a nucleic acid that is administered to the subject; wherein an ADNF I polypeptide of part (a) and an ADNF III polypeptide of part (b) are administered to the subject; wherein either or both active core sites of the ADNF I polypeptide and the ADNF III polypeptide comprise at least one D-amino acid; wherein either or both active core sites of the ADNF I polypeptide and the ADNF III polypeptide comprise all D-amino acids; wherein the ADNF I polypeptide is SEQ ID NO: 1 and wherein the ADNF III polypeptide is SEQ ID NO: 2; wherein the ADNF I polypeptide is a member of the group consisting of SEQ ID NO:1 and the ADNF III polypeptide is selected from the group consisting of SEQ ID NO: 2; wherein the ADNF I polypeptide comprises up to about 20 amino acids at at [sic] least one of the N-terminus and the C-terminus of the active core site of the ADNF I polypeptide and wherein the ADNF III polypeptide comprises up to about 20 amino acids at at [sic] least one of the N-terminus and the C-terminus of the active core site of the ADNF III polypeptide; wherein the subject has an autoimmune disease; wherein the ADNF polypeptide is administered to prevent an autoimmune disease; wherein the autoimmune disease is selected from the group consisting of Guillan-Barre syndrome; wherein the ADNF polypeptide is administered intanasally; wherein the ADNF polypeptide is administered orally; wherein the ADNF polypeptide is injected.

Gozes et al., (the '740 Patent) teach methods of using ADNF III polypeptides for the treatment and prevention of neurological deficiencies (abstract), including the amino acid sequence NAVPSIPQ (SEQ ID NO:6), [which is identical to instant SEQ ID NO: 2] and SALLRSIPA (SEQ ID NO: 5), [which is identical to instant SEQ ID NO: 1] (column 3, lines15-19 and 60-67; column 21, lines 15-18; column 44, lines 42-53; column 45, lines 32-). SALLRSIPA (SEQ ID NO: 5) is identified as an ADNF III polypeptide in the '740 Patent (column 20, lines 21-25). The protective effect of ADNF III polypeptides in preventing neuronal cell death is taught at column 3, lines 60-67. Full-length ADNF III is taught at column 3, lines 63-64. The administration of ADNF III polypeptides to prevent neuronal cell death associated with a number of other neurological diseases and deficiencies is taught at column 6, lines 33-36, and the use of ADNF III polypeptides to treat other neurological disorders is taught at column 6, lines 59-60. ADNF III variant polypeptides, including an ADNF III polypeptide comprising up to about 20 amino acids and at least one of the N-terminus and the C-terminus of the active core site are taught at column 3, lines 38-67 to column 4, lines 1-53; and column 45, lines 43-61; column 49, lines 47-49). Treatment of the neuro-autoimmune disease, Guillian-Barre syndrome, is taught at column 45, line 7. Amino acid sequences with naturally occurring amino acids and amino acid analogs, which include known analogues of natural amino acids that function in a manner similar to the naturally occurring amino acids (i.e. amino acid mimetics and analogs) are taught at column 5, lines 34-64. Administration of the ADNF III polypeptides systemically, intravenously, subcutaneously, intranasally, and orally are taught at column 45, lines 62-67 to column 46, lines 1-20; column 46, lines 31-37; and column 46, lines 60-65). The SALLRSIPA polypeptide, also identified as "ADNF-9" (at column 3, lines 60-61) is taught as being administered concurrently with "NAP" (NAPVSIPQ, SEQ ID NO: 6; taught as "NAP" at column 9, lines 6-7; column 7, line 44; column 59, lines 9-12) (column 60, lines 38-39). Administration of ADNF-14 (a polypeptide which comprises ADNF-9, see column 2, lines 63-64), ADNF-9, and NAP to mice are taught at Figure 16, column 10, lines 1-11; Figure 17, column 10, lines 12-23; and column 60, lines 31-53).

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 1, 9-11, 14-17, and 20-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Gozes et al., US Patent 6,613,740 (2 September 2003, priority to 7 February 1997) or WO 98/35042 (published 13 August 1998), in view of Brenneman et al., (US PreGrant Publication US 2002/001301 A1, published 15 August 2002).

The claims recite a method for preventing or treating an autoimmune disease in a subject, comprising administering to the subject a therapeutically effective amount of an Activity-Dependent Neurotrophic Factor (ADNF) polypeptide, wherein the ADNF polypeptide is a member selected from the group consisting of an ADNF polypeptide comprising an active core site having the following amino acid sequence: NAPVSIPQ (SEQ ID NO: 2) [as elected]; wherein the ADNF polypeptide is an ADNF III polypeptide; wherein the ADNF polypeptide is a full length ADNF III polypeptide; wherein the ADNF III polypeptide is SEQ ID NO: 2; wherein the active core site of the ADNF III polypeptide comprises at least one D-amino acid; wherein the active core site of the ADNF III polypeptide comprises all D-amino acids; wherein the ADNF III polypeptide is a member of the group consisting of SEQ ID NO: 2 [as elected]; wherein the ADNF III polypeptide comprises up to about 20 amino acids at at [sic] least one f the N-terminus and the C-terminus of the active core site; wherein at least one of the ADNF polypeptides is encoded by a nucleic acid that is administered to the subject; wherein an ADNF I polypeptide of part (a)

and an ADNF III polypeptide of part (b) are administered to the subject; wherein either or both active core sites of the ADNF I polypeptide and the ADNF III polypeptide comprise at least one D-amino acid; wherein either or both active core sites of the ADNF I polypeptide and the ADNF III polypeptide comprise all D-amino acids; wherein the ADNF I polypeptide is SEQ ID NO: 1 and wherein the ADNF III polypeptide is SEQ ID NO: 2; wherein the ADNF I polypeptide is a member of the group consisting of SEQ ID NO:1 and the ADNF III polypeptide is selected from the group consisting of SEQ ID NO: 2; wherein the ADNF I polypeptide comprises up to about 20 amino acids at at [sic] least one of the N-terminus and the C-terminus of the active core site of the ADNF I polypeptide and wherein the ADNF III polypeptide comprises up to about 20 amino acids at at [sic] least one of the N-terminus and the C-terminus of the active core site of the ADNF III polypeptide; wherein the subject has an autoimmune disease; wherein the ADNF polypeptide is administered to prevent an autoimmune disease; wherein the autoimmune disease is Guillan-Barre syndrome; wherein the ADNF polypeptide is administered intanasally; wherein the ADNF polypeptide is administered orally; wherein the ADNF polypeptide is injected.

Either of Gozes et al., (the '740 Patent) or WO 98/35042 teach methods of using ADNF III polypeptides for the treatment and prevention of neurological deficiencies (abstract), including the amino acid sequence NAVPSIPQ (SEQ ID NO:6), [which is identical to instant SEQ ID NO: 2] and SALLRSIPA (SEQ ID NO: 5), [which is identical to instant SEQ ID NO: 1] (column 3, lines15-19 and 60-67; column 21, lines 15-18; column 44, lines 42-53; column 45, lines 32-), as stated supra. Amino acid sequences with naturally occurring amino acids and amino acid analogs, which include known analogues of natural amino acids that function in a manner similar to the naturally occurring amino acids (i.e. amino acid mimetics and analogs) are taught at column 5, lines 34-64. However, neither Gozes et al. nor WO 98/35042, teaches the administration of ADNF nucleic acids.

Brenneman et al., teach the administration of ADNF polypeptides or nucleic acids by the recited means (p. 33, paragraph 0033) to treat conditions related to increased neuronal cell death (p. 1, paragraph 0003).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to make the perform the method of treating autoimmune disease in a subject by administering a therapeutically effective amount of an ADNF polypeptide, in polypeptide form as taught by Gozes et al., or in polypeptide form or nucleic acid form, as taught by Brenneman et al., and one would have reasonably expected success because Gozes et al., taught the administration ADNF peptides

as therapeutics to treat Guillan-Barre syndrome, and Brenneman et al., taught the use of ADNF polypeptides or nucleic acids to treat conditions related to increased neuronal cell death.

21. Claims 1, 9-15, and 17-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gozes et al., US Patent 6,613,740 (2 September 2003, priority to 7 February 1997) and WO 98/35042 (published 13 August 1998), in view of Voet et al., (1995 Biochemistry, 2nd Ed., p. 67) and Goodman et al., (US Patent 4,587,046, 6 May 1986).

The claims recite a method for preventing or treating an autoimmune disease in a subject, comprising administering to the subject a therapeutically effective amount of an Activity-Dependent Neurotrophic Factor (ADNF) polypeptide, wherein the ADNF polypeptide is a member selected from the group consisting of an ADNF polypeptide comprising an active core site having the following amino acid sequence: NAPVSIPQ (SEQ ID NO: 2) [as elected]; wherein the ADNF polypeptide is an ADNF III polypeptide; wherein the ADNF polypeptide is a full length ADNF III polypeptide; wherein the ADNF III polypeptide is SEQ ID NO: 2; wherein the active core site of the ADNF III polypeptide comprises at least one D-amino acid; wherein the active core site of the ADNF III polypeptide comprises all D-amino acids; wherein the ADNF III polypeptide is a member of the group consisting of SEQ ID NO: 2 [as elected]; wherein the ADNF III polypeptide comprises up to about 20 amino acids at at [sic] least one f the N-terminus and the C-terminus of the active core site; wherein at least one of the ADNF polypeptides is encoded by a nucleic acid that is administered to the subject; wherein an ADNF I polypeptide of part (a) and an ADNF III polypeptide of part (b) are administered to the subject; wherein either or both active core sites of the ADNF I polypeptide and the ADNF III polypeptide comprise at least one D-amino acid; wherein either or both active core sites of the ADNF I polypeptide and the ADNF III polypeptide comprise all D-amino acids; wherein the ADNF I polypeptide is SEQ ID NO: 1 and wherein the ADNF III polypeptide is SEQ ID NO: 2; wherein the ADNF I polypeptide is a member of the group consisting of SEQ ID NO:1 and the ADNF III polypeptide is selected from the group consisting of SEQ ID NO: 2; wherein the ADNF I polypeptide comprises up to about 20 amino acids at at [sic] least one of the N-terminus and the C-terminus of the active core site of the ADNF I polypeptide and wherein the ADNF III polypeptide comprises up to about 20 amino acids at at [sic] least one of the N-terminus and the C-terminus of the active core site of the ADNF III polypeptide; wherein the subject has an autoimmune disease; wherein the ADNF polypeptide is administered to prevent an autoimmune disease; wherein the autoimmune disease is selected from the group consisting of Guillan-Barre syndrome; wherein the ADNF

polypeptide is administered intanasally; wherein the ADNF polypeptide is administered orally; wherein the ADNF polypeptide is injected.

Gozes et al., (the '740 Patent) and WO 98/35042teach methods of using ADNF III polypeptides for the treatment and prevention of neurological deficiencies (abstract), including the amino acid sequence NAVPSIPQ (SEQ ID NO:6), [which is identical to instant SEQ ID NO: 2] and SALLRSIPA (SEQ ID NO: 5), [which is identical to instant SEQ ID NO: 1] (column 3, lines15-19 and 60-67; column 21, lines 15-18; column 44, lines 42-53; column 45, lines 32-), *supra.* Amino acid sequences with naturally occurring amino acids and amino acid analogs, which include known analogues of natural amino acids that function in a manner similar to the naturally occurring amino acids (i.e. amino acid mimetics and analogs) are taught at column 5, lines 34-64. However, Gozes et al., and WO 98/35042 do not specifically recite these amino acid mimetics and analogs as D-amino acids.

Voet et al., teach that D-amino acids are more resistant to proteases than their L-amino acid counterparts (p. 67).

Goodman et al., teach that incorporation of D-amino acids into peptides is particularly advantageous when those peptides are administered to patients, as the D-amino acids are resistant to proteolysis in vivo (column 9, lines 48-54).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make the perform the method of treating autoimmune disease in a subject by administering a therapeutically effective amount of an ADNF polypeptide, as taught by Gozes et al., and one would have reasonably expected success because Gozes et al., taught the administration ADNF peptides as therapeutics to treat Guillan-Barre syndrome, and Voet and Goodman taught the value of having one or more D-amino acids incorporated into a protein to be administered to a patient, as the incorporation of one or more D-amino acids would increase the stability of the protein when administered in vivo.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cherie M. Woodward whose telephone number is (571) 272-3329. The examiner can normally be reached on Monday - Thursday 9:00am-7:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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